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### New Licence Extension for RoACTEMRA in Europe

*RoACTEMRA now indicated to reduce the rate of progression of joint damage  
and improve physical function in rheumatoid arthritis*

Roche announced today that the European Commission (EC) has extended RoACTEMRA's indication to reduce the rate of progression of joint damage and improve physical function in patients with rheumatoid arthritis (RA), when given in combination with methotrexate (MTX). The licence extension comes just over a year after initial approval and further reinforces RoACTEMRA as an effective treatment for RA.

Joint damage in RA often begins early in the disease and can lead to permanent disability. Therefore, inhibiting this structural damage to patients' joints is a critical measure of the effectiveness of an RA treatment. For patients this means that they may be able to continue to enjoy their lives without the worsening disability usually associated with the disease.

The approval from the EC was based on positive two-year data from the phase III LITHE<sup>1</sup> trial. This trial demonstrated that patients receiving RoACTEMRA in combination with MTX had significantly less damage to their joints at two years, compared to patients in the control group. The outcome was determined by x-rays which measured over time the progression of bone erosions and narrowing of joint spaces. The data showed that with long-term use, patients with RA treated with RoACTEMRA 8mg/kg plus MTX suffered 81% less damage to their joints compared to those treated in the control group at week 104.

"The extended licence approval granted by the EC today is great news for patients," said Hal Barron, M.D, executive vice president, Global Development and chief medical officer. "This licence extension is based on robust Phase III data which not only demonstrates joint damage inhibition but consistently demonstrates high signs and symptoms remission rates across a range of RA patient types."

RoACTEMRA is currently licenced in Europe for use in combination with MTX, to treat adult patients with moderate to severe RA who responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor antagonists (anti-TNFs).<sup>2</sup> In these patients, RoACTEMRA can be given as monotherapy in cases of intolerance to MTX, or where continued treatment with MTX is inappropriate.<sup>2</sup>

RoACTEMRA (ACTEMRA as it is known in the US) was filed in the US in March 2010 for the prevention of structural joint damage and to improve physical function in adults with moderately to severely active RA. This filing followed ACTEMRA's approval by the FDA in January 2010 as the first humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody to treat adult patients with moderately to severely active RA who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies.

### **About the LITHE (Tocilizumab Safety and THE Prevention of Structural Joint Damage) study**

The LITHE study, a randomised, double-blind, placebo-controlled trial was designed to evaluate the efficacy of TCZ plus MTX in preventing structural joint damage and improving physical function over two years. LITHE was an international study, including 15 countries and 1196 patients with moderate to severe RA who had an inadequate response to MTX. In this randomised study, patients received either RoACTEMRA (4 mg/kg or 8 mg/kg, one infusion every four weeks) in combination with MTX or MTX alone. Results from the 24-month analysis showed that at 104 weeks, total Genant-modified Sharp Score change from baseline for the RoACTEMRA 8mg + MTX, 4mg +MTX, and MTX alone groups were: 0.37, 0.58 and 1.96 respectively. The HAQ-DI AUC change from baseline, adjusted mean scores were: -320.8, -287.5 and -139.4 respectively at 24 months.<sup>1</sup>

### **About RoACTEMRA/ACTEMRA**

RoACTEMRA/ACTEMRA is the result of research collaboration by Chugai and is also being co-developed globally with Chugai. RoACTEMRA/ACTEMRA is the first humanised interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. An extensive clinical development programme of five Phase III trials was designed to evaluate clinical findings of RoACTEMRA/ACTEMRA, all of which met their primary endpoints. RoACTEMRA/ACTEMRA was first approved in Japan, and launched by Chugai in June 2005 as a therapy for Castleman's disease; in April 2008, additional indications for rheumatoid arthritis (RA), juvenile idiopathic arthritis and systemic-onset juvenile idiopathic arthritis were also approved in Japan. RoACTEMRA/ACTEMRA was approved in the European Union in January 2009 for the treatment of RA in patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) inhibitors. It is also approved for use in several other countries, including India, Brazil, Switzerland, and Australia. RoACTEMRA/ACTEMRA was most recently (January 2010) approved in the United States for the treatment of adult patients with moderately to severely active RA who have had an inadequate response to one or more TNF inhibitors.

The overall safety profile of RoACTEMRA/ACTEMRA is consistent across all global clinical studies. The serious adverse events reported in RoACTEMRA/ACTEMRA clinical studies include serious infections, gastrointestinal perforations and hypersensitivity reactions including anaphylaxis. The most common adverse events reported in clinical studies were upper respiratory tract infection, nasopharyngitis, headache, hypertension and increased ALT. Increases in liver enzymes (ALT and AST) were seen in some patients; these increases were generally mild and reversible, with no

evidence of hepatic injuries or any observed impact on liver function. Laboratory changes, including increases in lipids (total cholesterol, LDL, HDL, triglycerides) and decreases in neutrophils and platelets, were seen in some patients without association with clinical outcomes. Treatments that suppress the immune system, such as ACTEMRA, may cause an increase in the risk of malignancies.

### **About Roche**

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and central nervous system (CNS). Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2009, Roche had over 80,000 employees worldwide and invested almost 10 billion Swiss francs in R&D. The Group posted sales of 49.1 billion Swiss francs. Genentech, United States, is a wholly owned member of the Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: [www.roche.com](http://www.roche.com).

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### **References:**

- 1) LITHE: tocilizumab inhibits radiographic progression and improves physical function in rheumatoid arthritis (RA) patients (Pts) at 2 years with increasing clinical efficacy over time. Fleischmann, R et al Oral presentation at the American College of Rheumatology (ACR), 18th October 2009
- 2) RoACTEMRA SmPC